REMARKS

This Amendment is responsive to the Office Action identified above, and is responsive in any other manner indicated below.

EXTENSIVE PROSECUTION NOTED

Applicant and the undersigned respectfully note the extensive prosecution which has been conducted to date with the present application, and thus Applicant and the undersigned respectfully request any help from the Examiner toward movement of the present application quickly to allowance.

NON-ACKNOWLEDGMENT OF CERTIFIED PRIORITY DOCUMENTS

Item 12c1 in the Office Action Summary indicates that none of the certified priority documents have been filed in the present application. Applicant respectfully **wholly traverses** this erroneous indication.

All five (5) of the certified priority documents for this application were timely filed on 16 November 2000. Attached is a copy of the Office date postcard indicating receipt of the documents on 16 November 2000, as well as a copy of the PAIR Image File Wrapper indicating (highlighted entry at the bottom of page 2) that such priority documents were entered in the present application. Further, acknowledgment of the priority documents already has been given, *e.g.*, in the Office Actions mailed 27 February and 20 November 2002.

Accordingly, Applicant respectfully submits that the indication of non-receipt of the priority documents is erroneous and contrary to the entire record for this case.

If the USPTO has misplaced any/all of the certified priority documents for the present application, Applicant **respectfully requests that the USPTO acknowledge such loss in writing, *i.e.*, that a Notice Under 37 CFR §1.251 be issued acknowledging receipt of the previously-filed certified priority documents** and requesting Applicant to file **second** copies of the certified priority documents be filed.

PENDING CLAIMS

Claims 1-11, 18-29 and 36-47 were pending, under consideration and subject to examination in the Office Action. Claim 1 has been amended merely to overcome a minor format informality. At entry of this paper, Claims 1-11, 18-29 and 36-49 will be pending for further consideration and examination in the application.

REJECTION UNDER 35 USC §103

All 35 USC §103 rejections of Claims 1-11, 18-29 and 36-47 are respectfully traversed. All descriptions of Applicant's disclosed and claimed invention, and all descriptions and rebuttal arguments regarding the applied prior art, as previously submitted by Applicant in any form, are repeated and incorporated herein by reference. Further, all Office Action statements regarding the prior art rejections are respectfully traversed. As additional arguments, Applicant respectfully submits the following.

Applicant's disclosed and claimed invention is directed to improved arrangements for inspecting a coupled state of hybridized target DNA on a DNA

chip. More particularly, in considering disadvantaged arrangements, Applicant found unacceptable inspection speeds, noise ratios and/or complexities.

For example, a disadvantaged arrangement using a scanning arrangement (*e.g.*, galvanometric or rotating mirror) to scan a **single** excitation spot across the area of a DNA chip's array, was found (by Applicant) to suffer a time penalty because inspection of probe cells of the array was (in essence) being conducted sequentially. Likewise, a disadvantaged arrangement using multiple pixels (*i.e.*, a sub-array) of a photomultiplier tube and/or CCD detector to detect each probe cell was found (by Applicant) to suffer unacceptable inspection speeds, noise ratios **and** complexities. More particularly, since any emitted light from a given probe cell was spread across (*i.e.*, detected by) multiple pixels, the light was shared (diluted) such that each pixel only received a portion of the emitted light and was more susceptible to noise interference (*e.g.*, scattered light, remnants of the excitation light). Further, the data from the multiple pixels (for any given probe cell) would then have to be analyzed/processed so as to come up with a single result value for the given probe cell. Such multiple pixel use/analysis was found (by Applicant) to represent unnecessary complexity and light dilution, leading to time penalties (due to processing) and/or detection errors (via noise).

In order to avoid the above problems, Applicant came up with a unique and novel combination invention using simultaneous scanning and detection of multiple probe cells at the same time (to improve speeds), and using one-to-one correspondence between probe cells, excitation light spots, and sensors (to eliminate complexities). That is, by simultaneously scanning and detecting, for

example, 10 probe cells, there can be a 10-fold increase in speed. By using one-to-one correspondence between probe cells, excitation light spots, and sensors, each probe cell is treated with a single excitation light spot and resultant emitted light is treated with a single sensor. Hence, light is concentrated to a single sensor (lessening noise sensitivity) and a probe cell detection value is immediately obtained from the single sensor (again improving speed).

In terms of claim language, independent claim 1, for example, recites "simultaneously irradiating a plurality of the DNA probe cells of said DNA chip with a corresponding plurality of multi-spot excitation lights through an objective lens so as to generate fluorescent lights from any fluorescently labeled target DNA hybridized to ones of the DNA probes of the plurality of DNA probe cells; ...and detecting said separate fluorescent lights simultaneously with a plurality of sensors, with each sensor corresponding to each of said DNA probe cells irradiated..." Other ones of Applicant's claims have similar and/or analogous limitations.

Of further interest, added independent claim 48 recites "simultaneously irradiating plural DNA probe cells out of said plurality of DNA probe cells of said DNA chip with a corresponding plurality of multi-spot excitation lights under a condition that each spot of said multi-spot excitation lights **corresponds** to a DNA probe cell through an objective lens so as to generate fluorescent lights from any fluorescently labeled target DNA hybridized to ones of the DNA probes of the plural DNA probe cells; ...and detecting said separate fluorescent lights simultaneously with a plurality of sensors, with each sensor **corresponding** to each of said DNA probe cells irradiated...".

Finally, added independent claim 49 recites "simultaneously irradiating a plurality of the DNA probe cells of said DNA chip with a corresponding plurality of multi-spot excitation lights under a condition that each spot of the multi-spot excitation lights **corresponds** to one DNA probe cell through an objective lens so as to generate fluorescent lights from any fluorescently labeled target DNA hybridized to ones of the DNA probes of the plurality of DNA probe cells; ...and detecting said separate fluorescent lights simultaneously with a corresponding plurality of sensors under a condition that each separate fluorescent light **corresponds** to one sensor...".

In order to properly support a §103 obviousness-type rejection, the reference not only must suggest the claimed features, but also must contain the motivation for modifying the art to arrive at an approximation of the claimed features. However, the cited art does not adequately support a §103 obviousness-type rejection.

More particularly, it is respectfully noted that rejection based on the first three (out of four) references had been previously overcome in Applicant's prior papers. That is, none of the three Pinkel *et al.*, Stern and Rosenberg references disclosed an arrangement where fluorescent lights generated simultaneously from a plurality of DNA probe cells are separately/simultaneously detected with separate detectors for each of the DNA probe cells.

That is, Pinkel *et al.* uses a standard fluorescence microscope arrangement and a CCD camera to acquire color images. Pinkel *et al.*'s sample is not a DNA probe. In Pinkel *et al.*, there is no disclosure that a plurality of DNA probe cells are irradiated simultaneously with multi-spot exciting lights, and that the generated and

separated fluorescent lights are simultaneously detected with a plurality of sensors each corresponding to each of the DNA probe cells irradiated.

Stern teaches the opposite of Applicant's invention, *i.e.*, teaches an arrangement having a scanning device which rapidly sweeps a single activation beam or spot across a surface of a substrate. Office Action comment cite Stern's column 10, lines 21-28, and quote "simultaneous interrogation of a single array with multiple target sequence" and "directing the fluorescent signal to detectors (applicant's sensor" such that the signal is detected, measured and recorded." A couple of points are critical to note in rebuttal. First, as mentioned above, Stern teaches scanning of a single spot. Next, in talking about "simultaneous interrogation of a single array", Stern's column 10 text is talking about using multiple dichroic mirrors to deflect different wavelengths of the returned excitation light. Accordingly, a single Stern apparatus can be commonly used to detect different wavelengths rather than having to use separate apparatus to detect different wavelengths.

The reference to Rosenberg relates to an operation tool using a laser beam through optical fibers. It does not even relate to an inspection of DNA probe. There is no disclosure that a plurality of DNA probe cells are irradiated simultaneously with multi-spot exciting lights, and that the fluorescent lights are detected with a plurality of sensors, each corresponding to each spot of the multi-spot exciting lights.

Now, the Examiner cites Rava *et al.* Rava *et al.* relates to arrangements for concurrently processing multiple biological chip assays, where a biological chip plate contains a plurality of test wells which each have a biological chip having a molecular probe array. Rava *et al.* teaches use of a monochromatic or polychromatic light

source in the form of a line of light (column 6, line 43) or scanning (of a single spot) using galvometric or polyhedral mirrors (column 6, lines 54-55). For detection, Rava *et al.*, for example, teaches use of a photomultiplier tube (column 5, lines 30-31, for example), or a CCD camera (column 6, lines 19-20, for example).

What Rava *et al.* (line Pinkel *et al.*, Stern and Rosenberg) does not teach, is simultaneously irradiating a plurality of the DNA probe cells of said DNA chip with a corresponding plurality of multi-spot excitation lights, or detecting separate fluorescent lights (which are returned along separate channels) simultaneously with a plurality of sensors, with each sensor corresponding to each of said DNA probe cells irradiated. More particularly, Rava *et al.*'s CCD arrangements, for example, uses 6 lines (column 6, lines 33-34) of an image to detect each feature (*e.g.*, a probe). Nowhere does Rava *et al.* talk about using multi-spots, or attributing a detector to returned emitted light from a given excitation spot.

To conclude, given that none of the applied references (taken alone or in combination) disclosed any arrangement even closely resembling Applicant's "simultaneously irradiating a plurality of the DNA probe cells of said DNA chip with a corresponding plurality of multi-spot excitation lights through an objective lens so as to generate fluorescent lights from any fluorescently labeled target DNA hybridized to ones of the DNA probes of the plurality of DNA probe cells; ...and detecting said separate fluorescent lights simultaneously with a plurality of sensors, with each sensor corresponding to each of said DNA probe cells irradiated...", it is respectfully submitted that no combination of such references would have disclosed or suggested Applicant's invention.

Further, since Stern relates to scanning with a single spot, such appears at least somewhat incompatible with Pinkel *et al.* and Rava *et al.* which appear mainly to image. Still further, it is respectfully noted that Rosenberg does not even relate to an inspection of DNA probe. Given that a significant number of seemingly incompatible/irrelevant references were used, it is respectfully submitted that this continued rejection of Applicant's invention based upon more-and-more references smack of an improper hindsight reconstruction approach to rejection.

In addition to the foregoing, the following additional remarks from Applicant's foreign representative are also submitted in support of traversal of the rejection and patentability of Applicant's claims.

None of the references of record disclose the following important features of the present invention:

1) a plurality of laser beams are simultaneously irradiated to a plurality of DNA probe cells, each of the laser beams corresponding to each of the DNA probe cells; and

2) fluorescent lights generated simultaneously from the plurality of DNA probe cells are separately detected for each of the plurality of DNA probe cells.

Pinkel *et al.*, at Col.12, lines 28-39, describes that a polychromatic beam splitter is used. In Pinkel *et al.*, correction of chromatic aberration is executed to prevent from the shifting of an image according to color. However, Pinkel *et al.* is very different from the art in which fluorescent lights generated simultaneously from the plurality of DNA probe cells are separately detected for each of the plurality of DNA probe cells. Further, in Pinkel *et al.*, there is no disclosure that a plurality of

laser beams are simultaneously irradiated to a plurality of DNA probe cells, and each of the laser beans corresponds to each of the DNA probe cells.

In the portion of Stern recited in the Office Action, it is described that fluorescent lights which are obtained by irradiation of argon laser are divided into two components above 515 nm and below 515 nm. However, again, Stern is very different from the art in which fluorescent lights generated simultaneously from the plurality of DNA probe cells are separately detected for each of the plurality of DNA probe cells. Further, in Stern, there is no disclosure that a plurality of laser beams are simultaneously irradiated to a plurality of DNA probe cells.

In Rosenberg, at Col. 19, it is described that multiple beams are irradiated to a target along with a reference light axis. However, this is executed to measure interference of a light having a particular wavelength (see, *e.g.*, Doppler analysis in Col. 18, lines 53-58). It is again noted that the art of Rosenberg is very different from the art in which a plurality of laser beams are simultaneously irradiated to a plurality of DNA probe cells. In Rosenberg, there is no disclosure concerning the art that fluorescent lights generated simultaneously from the plurality of DNA probe cells are separately detected for each of the plurality of DNA probe cells.

In Rava *et al.*, at Col. 6, lines 40-57, it is described that a laser beam is irradiated to a target in a linear manner, and scanning is executed in a stripe manner. However, this is very different from the present invention, and from a plurality of laser beans that are simultaneously irradiated to a plurality of DNA probe cells.

As is clear from the above, the present invention is very different from the references, and accordingly, the present invention is patentable thereover.

As a result of all of the foregoing, it is respectfully submitted that the applied art (taken alone and in the Office Action combinations) would not support a §103 obviousness-type rejection of Applicant's claims. Accordingly, reconsideration and withdrawal of such §103 rejection, and express written allowance of all of the §103 rejected claims, are respectfully requested. Further, at this point, it is respectfully submitted as a reminder that, if new art is now cited against any of Applicant's unamended claims, then it would not be proper to make a next Action final.

RESERVATION OF RIGHTS

It is respectfully submitted that any and all claim amendments and/or cancellations throughout prosecution of the present application are without prejudice or disclaimer of any scope or subject matter. Applicant respectfully reserves all rights to file related application(s) (including reissue applications) directed to any/all previously claimed limitations/features which have been subsequently amended or cancelled, or to any/all limitations/features not yet claimed *i.e.*, Applicant continues to maintain no intention or desire to dedicate or surrender any limitations/features.

EXAMINER INVITED TO TELEPHONE

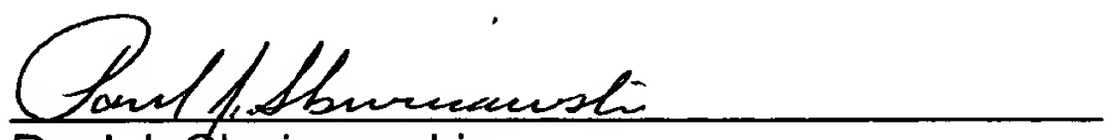
The Examiner is invited to telephone the undersigned at the local D.C. area number of 703-312-6600, to discuss an Examiner's Amendment or other suggested action for accelerating prosecution and moving the present application to allowance.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully submits that the claims listed above as presently being under consideration in the application are in condition for allowance. Accordingly, early allowance of such claims is respectfully requested.

A Petition for Extension of Time is submitted concurrently herewith. To whatever other extent is actually appropriate, Applicant respectfully petitions the Commissioner for an extension of time under 37 CFR §1.136. A Form PTO-2038 also is being filed concurrently herewith. Please charge any actual deficiency in appropriate fees due to ATS&K Deposit Account No. 01-2135 (as Case No. 500.39147X00).

Respectfully submitted,



Paul J. Skwierawski
Registration No. 32,173
ANTONELLI, TERRY, STOUT & KRAUS, LLP
1300 North Seventeenth Street, Suite 1800
Arlington, Virginia 22209-3873, USA
Telephone 703-312-6600
Facsimile 703-312-6666

Attachments:
Copy of 11/16/2000 Office Date Postcard
Copy of PAIR Image File Wrapper Printout

Concurrent Submissions:
Petition for Extension of Time
PTO-2038 (Fee Code 1251)

Patent ☒ Trademark ☐ 500.39147X00

Serial No. 09/678,652 Filed OCTOBER 4, 2000

Applicant(s) OSHIDA, ET AL.

Papers filed herewith on NOVEMBER 16, 2000

- ☐ Fees $ _____
- ☐ New Application
- ☐ Amendment
- ☐ Notice of Appeal
- ☐ Appeal Brief
- ☐ Other _____
- ☐ Assignment
- ☐ Letter to Draftsman
- ☒ Priority Documents
- ☐ Petition for Ext. of Time
- ☐ _____ Sheets of Formal Drawings

Receipt is hereby acknowledged of the papers filed as indicated in connection with above identified case.

COMMISSIONER OF PATENTS AND TRADEMARKS

PATENT APPLICATION INFORMATION RETRIEVAL

Image File Wrapper for Application No.:09/678,652

NEW Changes to IFW

This application is officially maintained in electronic form. To View: Click the desired Document Description. To Dow
the desired document(s) and click Download.

Mail Room Date	Document Description	Document Category	Page Count	All
11/19/2004	Bibliographic Data Sheet	PROSECUTION	2	
11/19/2004	List of references cited by Examiner	PROSECUTION	1	
11/19/2004	Non-Final Rejection	PROSECUTION	7	
11/19/2004	Search info on File Wrapper	PROSECUTION	1	
07/30/2004	Applicant Arguments or Remarks Made in an Amendment	PROSECUTION	2	
07/30/2004	Claim	PROSECUTION	20	
07/30/2004	Supplemental Response	PROSECUTION	2	
04/20/2004	Petition Decision	PROSECUTION	2	
03/17/2004	Fee Worksheet (PTO-875)	PROSECUTION	1	
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03/05/2004	Extension of time from Applicant - filed as separate letter	PROSECUTION	1	
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02/05/2004	Petition Entered	PROSECUTION	4	
01/09/2004	Miscellaneous Action with SSP	PROSECUTION	2	
11/24/2003	Miscellaneous Incoming Letter	PROSECUTION	4	
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11/05/2003	Final Rejection	PROSECUTION	8	
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10/28/2003	NPL Documents	PRIOR ART	2	
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05/15/2003	Advisory Action (PTOL-303)	PROSECUTION	3	
05/15/2003	Search info on File Wrapper	PROSECUTION	1	
04/21/2003	Applicant Arguments or Remarks Made in an Amendment	PROSECUTION	4	
04/21/2003	Notice of Appeal Filed	PROSECUTION	1	
04/21/2003	Claim	PROSECUTION	11	
04/21/2003	Amendment/Argument after Notice of Appeal	PROSECUTION	1	
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04/21/2003	Extension of time from Applicant - filed as separate letter	PROSECUTION	1	
11/20/2002	Final Rejection	PROSECUTION	7	
08/27/2002	Extension of time from Applicant - filed as separate letter	PROSECUTION	1	
08/27/2002	Applicant Arguments or Remarks Made in an Amendment	PROSECUTION	9	
08/27/2002	Amendment	PROSECUTION	13	
02/27/2002	Non-Final Rejection	PROSECUTION	9	
12/07/2001	Response to Election/Restriction Filed	PROSECUTION	3	
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07/17/2001	Request for Corrected Filing Receipt	PROSECUTION	2	
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11/16/2000	Foreign Priority Papers Filed	PROSECUTION	5	
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10/04/2000	Incoming Specification - Not in English	PROSECUTION	110	

10/04/2000	Drawings	PROSECUTION	58	
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10/04/2000	Foreign Reference	PRIOR ART	29	
10/04/2000	Miscellaneous Incoming Letter	AS FILED	171	
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